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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/002,443	01/02/98	SUTTER G	GSF97-06

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1631	12

DATE MAILED: 03/13/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/002,443	SUTTER ET AL.	
	Examiner	Art Unit	
	Mary K Zeman	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

1)☒ Responsive to communication(s) filed on *27 December 1999* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) *12-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11 and 31-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☒ None of the CERTIFIED copies of the priority documents have been:

1.☒ received.

2.☐ received in Application No. (Series Code / Serial Number) _____ .

3.☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

14) ☒ Notice of References Cited (PTO-892)
15) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
16) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6,8* .
17) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
18) ☐ Notice of Informal Patent Application (PTO-152)
19) ☐ Other: .

DETAILED ACTION

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1631.

Claims 1-34 are pending in this application. Claims 31-34 are newly added and are directed to elected group I.

Applicant's election with traverse of Group I, claims 1-11 in Paper No. 11 is acknowledged. The traversal is on the ground(s) that all of the groups require the recombinant viruses of Group I, the searching of all the Inventions would not constitute an undue burden, and that at most the Application should be split into only two groups, those two being the compositions and the methods. This is not found persuasive because each Invention, as set forth previously, is a distinct and separably patentable Invention. The various composition groups each comprise differing compositions of matter, having differing properties and different uses. While the methods of use all use a recombinant virus, each method has differing steps, and differing goals to be achieved. A method of preventing AIDS is quite different from a method of producing virus particles. A search for the method of preventing AIDS is unlikely to shed light on methods of preventing cancer. Finally, the Inventions are classified in a variety of classifications which do not substantially overlap.

The requirement is still deemed proper and is therefore made FINAL.

Claims 12-30 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 11.

Priority

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Denmark on 07/04/95, and a PCT Application filed 07/03/96. It is noted, however, that applicant has not filed a certified copy of the priority applications as required by 35 U.S.C. 119(b). It is noted that this application is a continuation of a PCT application. In these situations the International Bureau does **not** furnish copies of the priority documents.

Specification

The amendment filed 12/27/99 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: "wherein the site of the naturally occurring deletion is not site III".

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Objections

Claims 4-7 are objected to because of the following informalities:

Claims 4 and 5 recite improper Markush language. Claim 4 uses too many "or" clauses. An appropriate expression could be: "an antigenic determinant selected from the group consisting of A, B, C, and D."

Claim 6 has a typographical error "tryosinase", presumably "tyrosinase. Appropriate correction is required.

Claim Rejections - 35 USC § 112

Claims 1-11 and 31-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims recite a variety of abbreviations such as MVA, HIV, and TYR. The abbreviations should be spelled out at their first appearance in the claims. For example: "Modified vaccinia virus Ankara (MVA)".

Claim 11 is vague and indefinite as it is not clear whether Applicant intends the recombinant virus to be able to replicate in human cells, or whether the virus is to be free of virus which can replicate in human cells. Also, what are these other viruses? Where are they coming from?

Claims 1-11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention..

Claim 1 has been amended to exclude recombinant MVA viruses which have insertions in the site III locus. There is no basis for this negative limitation in the specification, as filed. The specification at page 5 identifies six major deletion loci in the MVA genome, but does not give any basis for the exclusion of insertions into site III. The whole of the specification is directed to recombinant MVA viruses wherein the insertion is at site II. There is no direct teaching that excludes insertions at site III, nor any reasons why one would exclude such insertions. This amendment is new matter, and must be canceled in response to this rejection. Applicant is reminded that any further amendments should avoid the prior art teachings of insertions into site III without introducing new matter.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-3, and 8-11 are rejected under 35 U.S.C. 102(a) as being anticipated by Sutter et al. (1995 FEBS Letters 371 p 9-12 August 28).

The above rejected claims are drawn to recombinant MVA viruses wherein the T7 RNA polymerase gene is inserted into a naturally occurring deletion in the host genome, deletion II.

Sutter (1995) discloses recombinant MVA viruses wherein the bacteriophage T7 RNA polymerase is inserted into the deletion II site. The T7 polymerase is under the direction of a vaccinia virus p7.5 promoter. This is exemplified in section 3.1, and figure 1. Perfection of Applicant's claim to foreign priority would obviate this rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5, and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Small Jr. et al. (US Patent 5,676,950).

Small Jr. et al. (US Patent 5,676,950) discloses recombinant MVA viruses wherein antigenic determinants from influenza or from HIV are inserted into a naturally occurring

deletion of the MVA virus. MVA is a preferred virus (column 2 lines 29-31), and is disclosed as having six naturally occurring deletion sites in the genome (column 6 lines 14-19). MVA is a preferred virus due to its extreme attenuation, yet unimpaired gene expression (column 6 lines 23-40). Various antigenic sequences are contemplated by Small Jr. et al., including hepatitis B antigens (example 4), influenza, measles, diphtheria, tetanus, pertussis, tuberculosis, cholera, and even polysaccharide mimics (column 5 lines 10-28). The recombinant virus is able to express the foreign gene such that animals vaccinated with the recombinant virus were able to generate an immune response to the expressed polypeptide (examples 6-8). The insertion of sequences expressing antigens of HIV proteins into recombinant vaccinia viruses is discussed in Example 4. Small Jr. et al. do not specifically identify which insertion site is used in their recombinant viruses.

It would have been obvious for one of ordinary skill in the art at the time the invention was made to have selected any one of the naturally occurring deletion sites of MVA for insertion of sequences encoding heterologous antigens. Small Jr. et al. disclose that MVA has six suitable sites for such insertions, and indicates that any site can be utilized. Heterologous antigens are effeciently expressed from the insertion sites, and such antigens can provide protection from homologous challenge. Small Jr. et al. disclose the suitability of several antigens for such expression, including antigens of viruses, bacteria and parasites. One would have been motivated to use the MVA virus because it is an excellent vaccine candidate due to its extreme attenuation, the availability of insertion sites, the level of gene expression, and the safety for laboratory workers.

Claims 6, 7, 31 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Small Jr. et al. (US Patent 5,676,950) as applied to claims 1-5 and 11 above, in view of Altenberger et al. (1989 PTO-1449 AZ) and further in view of Montagnier et al. (US Patent 5,221,610).

The above rejected claims are drawn to recombinant MVA viruses wherein a foreign gene, such as HIV nef, is inserted into a naturally occurring deletion. A preferred deletion site is deletion II.

Small Jr. et al. (US Patent 5,676,950) discloses recombinant MVA viruses wherein antigenic determinants from influenza or from HIV are inserted into a naturally occurring deletion of the MVA virus. MVA is a preferred virus (column 2 lines 29-31), and is disclosed as having six naturally occurring deletion sites in the genome (column 6 lines 14-19). MVA is a preferred virus due to its extreme attenuation, yet unimpaired gene expression (column 6 lines 23-40). Various antigenic sequences are contemplated by Small Jr. et al., including HIV gp120, gp160 and "other HIV proteins" (Example 4). The recombinant virus is able to express the foreign gene such that animals vaccinated with the recombinant virus were able to generate an immune response to the expressed polypeptide (examples 6-8). The insertion of sequences expressing antigens of HIV proteins into recombinant vaccinia viruses is discussed in Example 4. Small Jr. et al. do not specifically identify which insertion site is used in their recombinant viruses, nor do Small Jr. et al. specifically disclose the use of the HIV nef protein.

Altenberger et al. (1989) discloses recombinant MVA viruses. Altenberger et al. discloses the location of deletion II, (pages 18-20) and suggests that MVA recombinants can

express malaria antigens from genes inserted into this location. (page 25, second paragraph) Altenberger et al. also notes that recombinant MVA viruses having insertions into the deletion II area could potentially be used as vaccines (page 25, last paragraph). Altenberger et al. provides motivation to insert the foreign gene of interest into the deletion II region of MVA, in order to obtain foreign gene expression.

Finally, Montagnier et al. (US Patent 5,221,610) discloses the HIV nef protein, and nucleotides encoding nef, for use in producing recombinant nef polypeptides which can be used in HIV detection, and in immunogenic compositions. Montagnier et al. expresses the nef protein from recombinant vaccinia viruses (columns 13 and 14). These recombinant vaccinia viruses produce a nef polypeptide which is bound by sera from patients with AIDS. Montagnier et al. teaches that recombinant vaccinia viruses can express antigenic nef polypeptides.

It would have been obvious for one of ordinary skill in the art at the time the invention was made to have selected any one of the naturally occurring deletion sites of MVA, including site II, for insertion of sequences encoding heterologous antigens. Small Jr. et al. disclose that MVA has six suitable sites for such insertions, and indicate that any site can be utilized. Both Altenberger et al. and Small Jr. et al. disclose that heterologous antigens are efficiently expressed from the insertion sites, and such antigens can provide protection from homologous challenge. Small Jr. et al. disclose the suitability of several antigens for such expression, including antigens of HIV for use in recombinant MVA viruses. One of skill in the art would have been motivated to select the nef gene of HIV in view of the disclosure of Montagnier et al., which indicates that immunogens comprising nef proteins are highly desirable for vaccine compositions against

AIDS. One of skill in the art would have been further motivated to use the MVA virus because it is an excellent vaccine candidate due to its extreme attenuation, the availability of insertion sites, the level of gene expression, and the safety for laboratory workers.

Therefore, the invention as a whole is *prima facie* obvious, absent evidence to the contrary.

Claims 6, 7, and 33-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Small Jr. et al. (US Patent 5,676,950) as applied to claims 1-5 and 11 above, in view of Altenberger et al. (1989 PTO-1449 AZ) and further in view of Kwon (US Patent 5,679,511).

The above rejected claims are drawn to recombinant MVA viruses wherein a foreign gene, such as human tyrosinase, is inserted into a naturally occurring deletion. A preferred deletion site is deletion II.

Small Jr. et al. (US Patent 5,676,950) discloses recombinant MVA viruses wherein antigenic determinants from various heterologous genes can be inserted into a naturally occurring deletion of the MVA virus. MVA is a preferred virus (column 2 lines 29-31), and is disclosed as having six naturally occurring deletion sites in the genome (column 6 lines 14-19). MVA is a preferred virus due to its extreme attenuation, yet unimpaired gene expression (column 6 lines 23-40). Small Jr. et al. disclose that the recombinant MVA viruses can be used in cancer prevention (column 5 line 21) using appropriate antigens. The recombinant MVA virus of Small Jr. et al. is able to express the foreign gene such that animals vaccinated with the recombinant virus were able to generate an immune response to the expressed polypeptide (examples 6-8).

Small Jr. et al. do not specifically identify which insertion site is used in their recombinant viruses, nor do Small Jr. et al. specifically disclose the use of the tyrosinase gene.

Altenberger et al. (1989) discloses recombinant MVA viruses. Altenberger et al. discloses the location of deletion II, (pages 18-20) and suggests that MVA recombinants can express malaria antigens from genes inserted into this location. (page 25, second paragraph) Altenberger et al. also notes that recombinant MVA viruses having insertions into the deletion II area could potentially be used as vaccines (page 25, last paragraph). Altenberger et al. provides motivation to insert the foreign gene of interest into the deletion II region of MVA, in order to obtain foreign gene expression.

Finally, Kwon (US Patent 5,679,511) discloses the cDNA sequence encoding human tyrosinase, and the expression of that protein from bacteriophage vectors. Kwon indicates that human tyrosinase is very important for understanding pigment disorders, and cancers such as melanomas. Kwon provides motivation to use the tyrosinase gene as an antigen as it is involved in melanomas, and could be a vaccine antigen.

It would have been obvious for one of ordinary skill in the art at the time the invention was made to have selected any one of the naturally occurring deletion sites of MVA, including site II, for insertion of sequences encoding heterologous antigens. Small Jr. et al. disclose that MVA has six suitable sites for such insertions, and indicate that any site can be utilized. Both Altenberger et al. and Small Jr. et al. disclose that heterologous antigens are efficiently expressed from the insertion sites, and such antigens can provide protection from homologous challenge. Small Jr. et al. disclose the use of recombinant MVA viruses for cancer prevention when the

proper cancer antigen is provided. Kwon provides that antigen, human tyrosinase, and indicates it could be used in a melanoma vaccine. One of skill in the art would have been further motivated to use the MVA virus because it is an excellent vaccine candidate due to its extreme attenuation, the availability of insertion sites, the level of gene expression, and the safety for laboratory workers.

Therefore, the invention as a whole is *prima facie* obvious, absent evidence to the contrary.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary K Zeman whose telephone number is (703) 305-7133. The examiner can be reached between the hours of 7:30 am and 5:00 pm Monday through Thursday, and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached at (703) 308 4028.

The fax number for this Art Unit is (703) 305-7401.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

mkz
March 7, 2000

MICHAEL P. WOODWARD
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